

We claim:

1. A thermal adhesion granulation process for preparing direct tableting formulations or aids, comprising the step of subjecting all or part of a mixture comprising:

A) from about 5 to about 99% by weight of one or more diluent excipients and/or from 0 to about 99% by weight of a pharmaceutically-active ingredient;

B) from about 1 to about 95% by weight of a binder excipient; and

optionally with,

C) from 0 to about 10% by weight of a disintegrant excipient;

to heating at a temperature range of from about 30 to about 130°C under the condition of from about 0.1 to about 20% initial moisture content and/or from about 0.1 to about 20% initial content of a pharmaceutically-acceptable organic solvent in a closed system under mixing by tumble rotation until the formation of granules.

2. A process as defined in claim 1, wherein the temperature range is from about 40 to about 110°C.

3. A process as defined in claim 1, wherein the temperature range is from about 60 to about 105°C.

4. A process as defined in claim 1, wherein the initial moisture content is from about 2 to about 15%.

5. A process as defined in claim 1, wherein the initial moisture content is from about 4 to about 10%.

6. A process as defined in claim 1, wherein the initial organic solvent content is from about 0.1 to about 10%.

7. A process as defined in claim 1, where the initial organic solvent content is from about 0.5 to about 5%.

8. A process as defined in claim 1, wherein the diluent excipient is powdered cellulose, microcrystalline cellulose, lactose, starch, or dibasic calcium phosphate.

9. A process as defined in claim 1, wherein the pharmaceutically-active ingredient is acetaminophen or ascorbic acid.
10. A process as defined in claim 1, wherein the binder excipient is soluble polyvinyl pyrrolidone or hydroxypropylcellulose.
- 5 11. A process as defined in claim 1, wherein the disintegrant excipient is crospovidone, sodium starch glycolate, reticulated carboxymethylcellulose, or low-substituted hydroxypropylcellulose.
12. A process as defined in claim 1, wherein the diluent excipient is microcrystalline cellulose.
- 10 13. A process as defined in claim 12, wherein the microcrystalline cellulose is of a type in which about 90% of the particles are in the range from about 1  $\mu\text{m}$  to about 125 $\mu\text{m}$ , and the average particle size is from about 10 $\mu\text{m}$  to about 70 $\mu\text{m}$ .
14. A process as defined in claim 1, wherein the binder excipient is soluble polyvinyl pyrrolidone.
- 15 15. A process as defined in claim 14, wherein the soluble polyvinyl pyrrolidone has a K value of from about 12 to about 120.
16. A process as defined in claim 14, wherein the soluble polyvinyl pyrrolidone has a K value of from about 20 to about 95.
17. A process as defined in claim 14, wherein the soluble polyvinyl pyrrolidone has a K value of from about 25 to about 35.
- 20 18. A process as defined in claim 1, wherein the binder excipient further contains from 0 to about 10% (by weight with respect to the binder) of an anticaking agent.
19. A process as defined in claim 18, wherein the binder excipient contains from about 0.01 to about 10% (by weight with respect to the binder) of an anticaking agent.
- 25 20. A process as defined in claim 18, wherein the binder excipient contains from about 2 to about 4% (by weight with respect to the binder) of an anticaking agent.
21. A process as defined in claim 18, wherein the anticaking agent is dibasic calcium phosphate anhydrous.

22. A product of thermal adhesion granulation process for preparing direct tableting formulations or aids as defined in claim 1.

23. A powder mixture of soluble polyvinyl pyrrolidone containing from about 0.01 to about 10% (by weight with respect to the polyvinyl pyrrolidone) of dibasic calcium phosphate anhydrous.

24. A direct tableting formulation or aid comprising:

i) from about 5 to about 99% by weight of powder cellulose, microcrystalline cellulose, lactose, starch, or dibasic calcium phosphate;

ii) from 0 to about 99% by weight of acetaminophen or ascorbic acid;

iii) from about 1 to about 95% by weight of a soluble polyvinyl pyrrolidone which contains from about 0.01 to about 10% (by weight with respect to the polyvinyl pyrrolidone) of dibasic calcium phosphate anhydrous; and

iv) from 0 to about 10% by weight of crospovidone, sodium starch glycolate, reticulated carboxymethylcellulose, or low-substituted hydroxypropylcellulose.